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Tissue adhesive and adhesive tape for pediatric wound closure: A systematic review and meta-analysis☆,☆☆

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A B S T R A C T

Background: Tissue adhesive (TiA), adhesive tape (AdT), and sutures can be used to close surgical wounds and lacerations in children. However, it is unclear which technique produces the best results.
Methods: In this prospectively registered study, the PubMed, Ovid MEDLINE, Cochrane Library, Centre for Reviews and Dissemination Database, and ScienceDirect databases were searched. English language studies published between January 1980 and August 2017 evaluating TiA and/or AdT for primary skin closure of surgical wounds or lacerations in patients aged ≤18 years were included. Study endpoints included clinician-rated wound cosmesis and incidence of wound complications.
Results: Thirty-one studies were included in the systematic review and 16 studies in the meta-analysis. Amongst heterogeneous studies, AdT yielded marginally better cosmetic outcomes than TiA ($p = 0.04$). There was no difference in cosmesis between sutured wounds and those closed with TiA ($p = 0.2$). No difference in overall risk of wound infection or dehiscence was identified when comparing TiA with AdT ($p = 0.3$), and TiA with sutures ($p = 0.9$ and 0.3 respectively).
Conclusions: TiA, AdT, and sutures can all be used for wound closure with equivalent risk of wound infection and dehiscence. AdT appears to convey better cosmesis. Further adequately powered studies directly comparing techniques are required.
Levels of Evidence: Level IV.

Contents

Abbreviations: TiA, Tissue adhesive; AdT, Adhesive tape; VAS, Visual Analogue Scale; HWES, Hollander Wound Evaluation Scale; RR, Risk ratio; SDM, Standard difference in mean; CI, Confidence interval.

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Although sutures have traditionally been used for wound closure, tissue adhesive (TiA) and adhesive tape (AdT) can also be utilized. However, there is little evidence to demonstrate which of these techniques produces superior outcomes [1].

TiA (adhesive glue), refers to the cyanoacrylate group of compounds. The liquid TiA polymerizes into a waterproof film upon contact with moisture or blood on the skin, bonding apposed edges together [2,3]. AdT has been used for centuries to achieve wound edge apposition [1]. However, the use of AdT without adjunctive tension-relieving sutures is typically limited to relatively immobile, low-tension wounds due to the low tensile strength the tape conveys [4,5].

TiA and AdT can also be used either as an adjunct to sutures for additional wound strength or as a dressing [6,7]. Both have been used for the management of surgical wounds and lacerations in children [8,9] but it remains unclear which yields the best outcomes. The aim of this systematic review and meta-analysis was to ascertain which of these techniques yields optimal results in children for closure of surgical wounds and lacerations. Our primary outcome was clinician-rated wound cosmesis. Secondary outcomes included incidence of wound infection and wound dehiscence, other complications, and cost.

1. Material and methods

1.1. Review registration

Registration with PROSPERO was attained (CRD42017071667). The PubMed, Ovid MEDLINE, Cochrane Library, Centre for Reviews and Dissemination Database, and ScienceDirect databases were independently searched by two investigators (ST and MS). References of included articles and relevant review articles were screened to identify additional publications. Appendix A summarizes the full search strategy.

1.2. Inclusion and exclusion criteria

All English language studies published after January 1980 evaluating the use of TiA and/or AdT for primary skin closure in children (≤18 years old) were considered for inclusion. Randomized controlled trials, retrospective and prospective case series were included. Studies with <10 patients, abstracts, animal research studies, book chapters, comments, letters, and review articles were excluded. Penile and contaminated surgical wounds were excluded.

1.3. Abstract screening

All identified abstracts were independently screened by two investigators (ST and MS) and relevant data extracted from the full-text articles. Discrepancies were resolved in discussion with the senior authors (MP and RN). Studies with overlapping data had only the first published study included. Quality of included studies was assessed using the Newcastle-Ottawa Scale for non-comparative studies and the Cochrane Risk of Bias Tool for comparative studies. Both primary and secondary endpoints were evaluated in the systematic review. Overall incidence of wound complications (infection/dehiscence/other) was pooled. The meta-analysis included data from comparative studies for cosmesis, wound infection, and wound dehiscence.

1.4. Wound complication definitions and standardization of data

Wound infection was included when directly reported or if antibiotics were prescribed on clinical review. Wound dehiscence was included when directly reported or if wound edge separation or gaping was described. Due to heterogeneity, any other reported issue including the requirement for repeat surgery was classified as 'Other complications". For the purposes of the meta-analysis, for articles reporting raw data for cosmesis using the visual analogue scale (VAS) or Hollander Wound Evaluation Scale (HWES), data were converted onto a consistent scale with all VAS data being converted to a 100-point scale (100 = best cosmesis) and HWES being converted so that 6 was the optimal score. In studies where cosmesis was scored more than once (i.e. two assessors/time-points of assessment/assessment scales), both were included in the meta-analysis.

1.5. Statistical analysis

Meta-analysis was conducted using Comprehensive Meta-Analysis Version 2 (Biostat, Inc., USA) and MedCalc 19 (MedCalc Software bvba, Ostend, Belgium). The random-effects model was used to produce risk ratios (RR) for categorical variables, and standard difference in mean (SDM) for continuous variables, along with 95% confidence intervals [CI]. The I^2 value was used to assess heterogeneity with $I^2 > 50\%$ representing substantial heterogeneity. Studies having no events in both arms were excluded from the analysis as per the Cochrane Handbook for Systematic Reviews of Interventions [10]. The funnel plot method and the Egger's regression test were used to assess for publication bias. p-values <0.05 were considered significant.

2. Results

2.1. Search results

Search results are reported in Fig. 1. Twenty-one comparative and 10 non-comparative studies were included with 16 comparative studies contributing to the meta-analysis. Sixteen comparative studies were

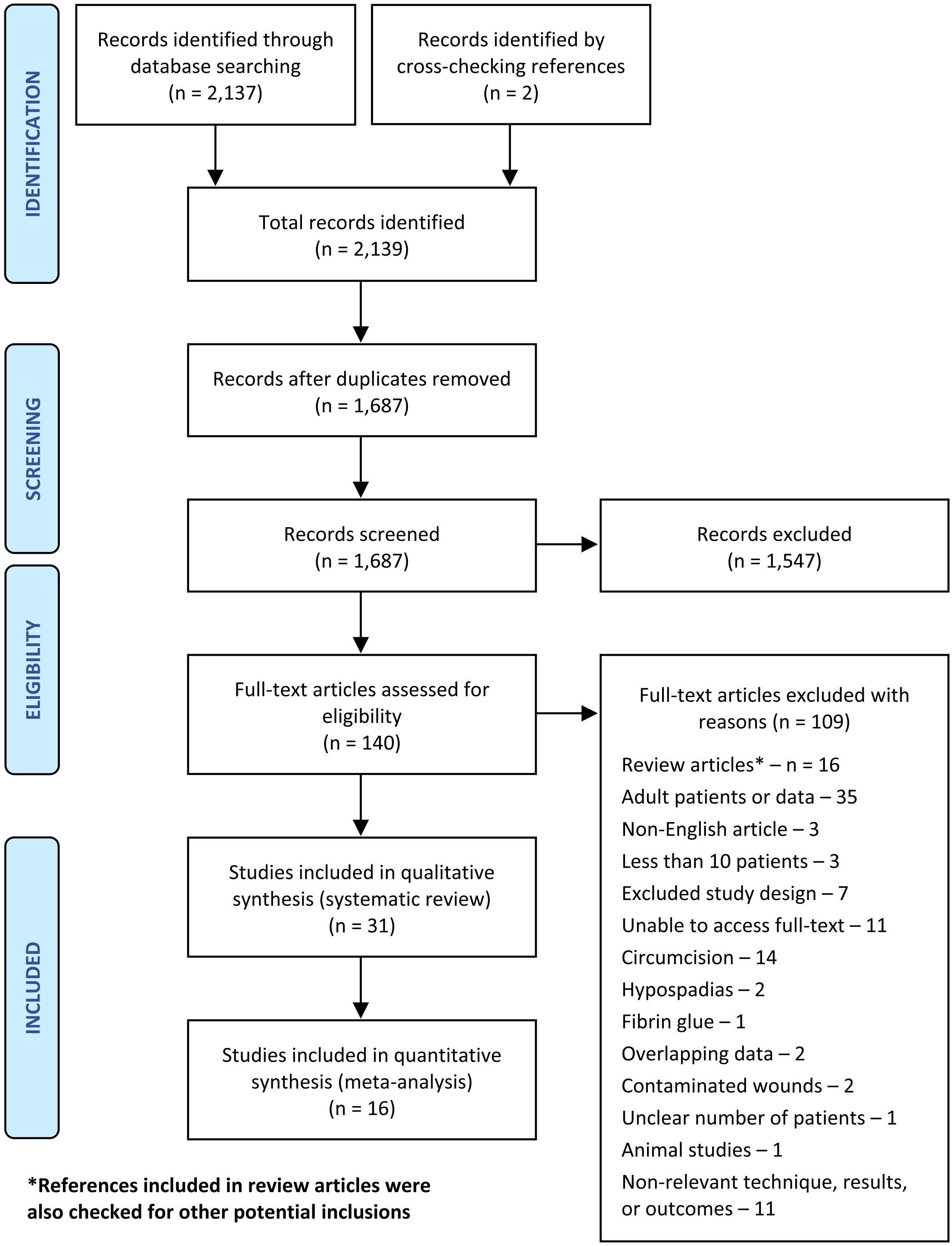

Fig. 1. Flowchart of included studies.

prospective (12 randomized, 4 non-randomized), four were retrospective, and the final study reported a cost analysis comparing closure techniques. Wounds closed were surgical in nature in 19 studies, lacerations in 11 studies, or both in 1 study.

There were a total of 9387 wounds: 8518 closed with TiA (5298 surgical wounds and 3220 lacerations), 303 closed with AdT (225 surgical wounds and 78 lacerations), and 566 closed with sutures (415 surgical wounds and 151 lacerations). In 9 studies, adjunctive TiA and/or AdT was applied to the wound after the skin was closed with sutures. In one of these studies, wounds closed with AdT had adjunct suture placement, but wounds closed with TiA did not additionally utilize sutures.

For wounds closed with TiA, octyl-cyanoacrylate (n = 992), butyl-cyanoacrylate (n = 7396), and isoamyl-cyanoacrylate (n = 130) were used. For wounds closed with AdT, Steri-Strips™ were used for 276 wounds; it was not stated what material was used for the remaining 27 wounds.

2.2. Quality of included studies

Overall, included studies were at high risk of bias. Results of this analysis are summarized in Tables 1 and 2.

Table 1
Quality of included comparative studies as assessed using the Cochrane Risk of Bias Tool.

Author	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Ademuyiwa et al. (2009) [12]	High	Some concerns	Low	High	Low	High
Anatol et al. (1997) [13]	High	Some concerns	Low	Low	Low	High
Barnett et al. (1998) [14]	High	Some concerns	Low	High	Low	High
Bernard et al. (2001) [15]	High	Some concerns	Low	Some concerns	Low	High
Brown et al. (2009) [16]	High	Some concerns	Low	Some concerns	Low	High
Bruns et al. (1996) [17]	High	Some concerns	Low	Low	Low	High
Bruns et al. (1998) [11]	High	Some concerns	Low	Some concerns	Low	High
Collin et al. (2009) [18]	High	Some concerns	Low	High	Low	Hgh
Doraiswamy et al. (2003) [19]	High	High	Low	High	Low	High
Ferlise et al. (2001) [20]	High	Some concerns	High	High	High	High
Halli et al. (2012) [21]	High	Some concerns	Low	Low	Low	High
Knott et al. (2007) [22]	High	Some concerns	Low	High	Low	High
Mattick et al. (2002) [9]	High	Some concerns	Low	Low	Low	High
Ong et al. (2002) [23]	High	Some concerns	Low	Low	Low	High
Osmond et al. (1999) [24]	Some concerns	Some concerns	Low	Low	Low	Some concerns
Osmond et al. (1995) [25]	High	Some concerns	Low	Some concerns	Low	High
Quinn et al. (1993) [26]	Some concerns	Some concerns	Low	Some concerns	Low	Some concerns
Romero et al. (2011) [8]	High	Some concerns	Low	Some concerns	Low	High
Spauwen et al. (2006) [27]	High	Some concerns	Low	High	Low	High
van den Ende et al. (2004) [28]	High	Some concerns	Low	Some concerns	Low	High
Wilson and Mercer (2008) [29]	High	Some concerns	Low	Some concerns	Low	High
Zempsky et al. (2004) [30]	Low	High	Low	High	Low	High

Table 2
Quality of included non-comparative studies as assessed using the Newcastle-Ottawa Scale.

Author	Selection (Max. of 4 Stars)	Comparability (Max. of 1 Star)	Exposure/Outcome (Max. of 3 Stars)	Overall Stars (Out of 8 Stars)
Elmasalme et al. (1995) [31]	2 stars	0 stars	2 stars	4 stars
Malhotra et al. (2016) [32]	1 star	0 stars	2 stars	3 stars
Amiel et al. (1999) [33]	1 star	0 stars	2 stars	3 stars
Hasan et al. (2009) [34]	1 star	0 stars	0 stars	1 star
Magee et al. (2003) [35]	1 star	0 stars	2 stars	3 stars
Mourougayan (2006) [36]	1 star	0 stars	2 stars	3 stars
Rajimwale et al. (2004) [7]	1 star	0 stars	1 star	2 stars
Resch & Hick (2000) [37]	2 stars	0 stars	2 stars	4 stars
Watson (1989) [38]	1 star	0 stars	1 star	2 stars

2.3. Clinician-rated cosmesis

Cosmesis was heterogeneously reported with different assessment scales used and variable time of cosmetic assessment post-operatively.

2.3.1. Non-comparative studies (n = 6 studies, 412 wounds)

Cosmesis was reported as favorable or satisfactory for most wounds in included studies [7,32,35,36,38]. One comparative study showed equivalent outcomes in TiA and sutured/stapled wounds [17]. Four studies did not report cosmesis assessment method [7,35,36,38].

2.3.2. TiA vs. AdT (n = 4 studies, 225 wounds)

Three studies showed no significant difference in cosmesis between groups [9,30] but one study did not describe assessment method [20]. The final study reported significantly better cosmesis with use of AdT [8]. Three studies (n = 173 wounds) were included in the meta-analysis (Fig. 2) [8,9,30]; two of these studies evaluated lacerations whilst the third assessed laparoscopic trocar wounds. Cosmetic outcome favored closure with AdT (SDM -0.39 [CI: −0.77–0.01], p = 0.04). Egger's regression test did not show significant publication bias (p = 0.8).

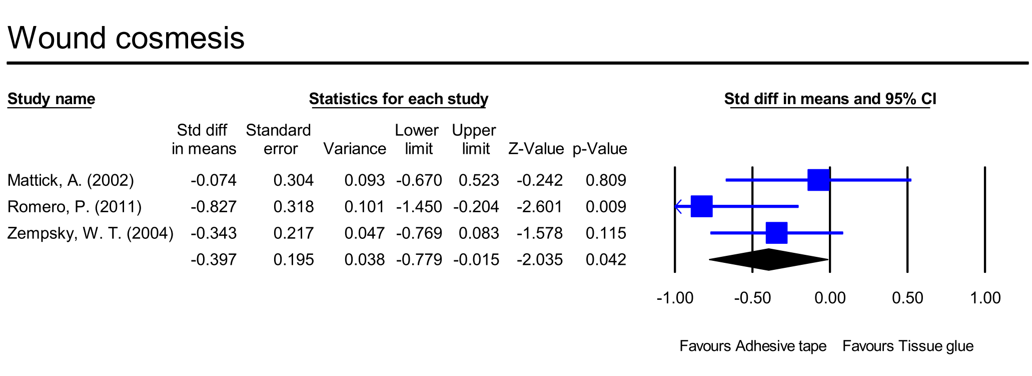

Fig. 2. Forest plot comparing wound cosmesis between TiA and AdT.

Wound cosmesis

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ademuyiwa, A. O. (2009)	-0.243	0.281	0.079	-0.794	0.308	-0.864	0.388
Bernard, L. (2001)1	-0.481	0.282	0.080	-1.034	0.072	-1.705	0.088
Bernard, L. (2001)	-0.669	0.286	0.082	-1.229	-0.108	-2.339	0.019
Brown, J.K. (2009)1	-0.188	0.173	0.030	-0.527	0.152	-1.082	0.279
Brown, J.K. (2009)	-0.117	0.173	0.030	-0.456	0.222	-0.676	0.499
Bruns, T.B. (1996)1	0.087	0.271	0.073	-0.444	0.618	0.320	0.749
Bruns, T.B. (1996)	0.543	0.276	0.076	0.003	1.084	1.970	0.049
Collin, T.W. (2009)	-0.361	0.451	0.203	-1.245	0.523	-0.801	0.423
Halli, R. (2012)	0.517	0.262	0.069	0.002	1.031	1.969	0.049
Knott, P.D. (2007)1	-0.043	0.426	0.182	-0.879	0.792	-0.102	0.919
Knott, P.D. (2007)	0.351	0.430	0.185	-0.491	1.193	0.817	0.414
Quinn, J. V. (1993)1	-0.175	0.231	0.054	-0.629	0.278	-0.758	0.448
Quinn, J. V. (1993)	-0.071	0.231	0.053	-0.524	0.382	-0.307	0.759
Spauwen, P.H.M. (2006)	0.032	0.365	0.133	-0.683	0.748	0.089	0.929
van den Ende, E. D. (2004)	-0.679	0.206	0.042	-1.082	-0.275	-3.299	0.001
	-0.121	0.096	0.009	-0.308	0.067	-1.258	0.208

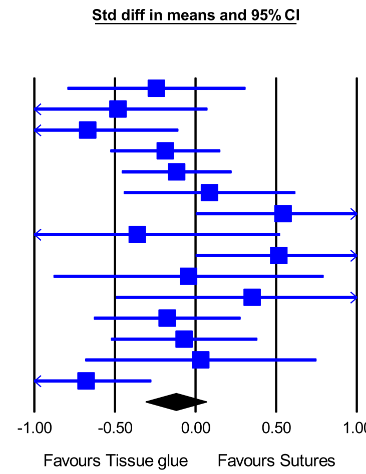

Fig. 3. Forest plot comparing wound cosmesis between TiA and sutures.

2.3.3. TiA vs. sutures (n = 12 studies, 723 wounds)

There was marked heterogeneity amongst studies with no significant difference [11,13,15,18,22,26,27], similar results [23], significantly improved cosmesis in wounds closed with TiA [21] or better cosmesis with sutures [14,28]. Results were split in the final study: one assessor found better cosmesis with TiA whilst another assessor found no difference [16]. Ten studies (n = 599 wounds) were included in the meta-analysis [11,14–16,18,21,22,26–28] with 5 studies having a second cosmetic assessor or reassessment of cosmesis at a second time-frame [14–16,22,26]. Cosmetic outcome was not different between TiA and sutures (Fig. 3) (SDM -0.12 [CI: 0.3–0.06], p = 0.2). Egger's regression test did not show significant publication bias (p = 0.4).

2.3.4. AdT vs. sutures (n = 1 study, 124 wounds at final follow-up)

It was unclear whether a difference existed due to conflicting results at different assessment time-points with no reported statistical significance at final assessment [12].

2.3.5. TiA vs. TiA (n = 1 study, 83 wounds)

There was no significant difference in wound cosmesis between groups (p = 0.84) [24].

2.4. Wound infection

Wound infection incidence was reported by 28 studies and overall rates are summarized in Table 3.

2.4.1. TiA vs. AdT (n = 5 studies, 543 wounds)

There was significant heterogeneity with no infections or no difference in wound infection rate [9,20,30], significantly more infections in the AdT group [29], or lack of clarity of a significant difference [8]. Three studies (n = 447 wounds) were included in the meta-analysis (Fig. 4) [8,29,30]. Incidence of wound infections was not different between the two groups (RR 0.3 [CI: 0.03–3.3]; p = 0.3) with homogeneity between the studies (I^2 = 36.9%; p = 0.2). Egger's regression test did not show significant publication bias (p = 0.3).

2.4.2. TiA vs. sutures (n = 12 studies, 792 wounds)

The majority reported no infections [14,15,18,22,23,27], with some no significant difference [26,28] or significantly more infections in the suture group [21]. The remaining three studies did not clarify if there was a significant difference in wound infection incidence [11,13,16]. Six studies (n = 459 wounds) were included in the meta-analysis (Fig. 5) [11,13,16,21,26,28]. Incidence of wound infections were similar between the two groups (RR 0.9 [CI: 0.3–2.6]; p = 0.9) with homogeneity between the studies (I^2 = 0.0%; p = 0.5). Egger's regression test did not show significant publication bias (p = 0.4).

2.4.3. AdT vs. sutures (n = 1 study)

The included study did not report wound infection incidence [12].

2.4.4. TiA vs. TiA (n = 1 study, 82 wounds)

There were no instances of wound infection reported [24].

2.5. Wound dehiscence

Incidence of wound dehiscence was reported by 27 studies and overall rates are summarized in Table 3.

2.5.1. TiA vs. AdT (n = 5 studies, 543 wounds)

The majority reported no dehiscence [8,9,20,29] with no significant difference in complication rate in the final study [30]. Due to non-events in both intervention arms amongst several included studies, there was not enough data available for meta-analysis.

2.5.2. TiA vs. sutures (n = 12 studies, 792 wounds)

The majority reported no wound dehiscence [11,13–15,18,21–23,27]. The others found no significant difference [26], did not clarify statistical significance [16] or dehiscence more likely to occur with TiA [28]. Three studies (n = 236 wounds) were included in the meta-analysis (Fig. 6) [16,26,28]. The incidence of dehiscence was not different between the two groups (RR 3.1 [CI: 0.3–24.0]; p = 0.3) with some homogeneity between the studies (I^2 = 55.6%; p = 0.1). Egger's regression test did not show significant publication bias (p = 0.6).

2.5.3. AdT vs. sutures (n = 1 study; 187 wounds)

More wound dehiscence occurred in the AdT group but the statistical significance of this was not reported [12].

2.5.4. TiA vs. TiA (n = 1 study; 82 wounds)

There was no significant difference in dehiscence incidence between groups (p = 0.50) [24].

Table 3
Rate of wound infection and wound dehiscence in included studies based on skin closure technique.

Study	Wound type/s	Tissue adhesive			Adhesive tape			Sutures		
		Total no. of wounds (n)*	No. of wound infections (n)	No. of wound dehiscences (n)	Total no. of wounds (n)*	No. of wound infections (n)	No. of wound dehiscences (n)	Total no. of wounds (n)*	No. of wound infections (n)	No. of wound dehiscences (n)
Ademuyiwa et al. (2009) [12]	Surgical wounds	26	0	0	-	-	-	26	1	0
Amiel et al. (1999) [33]	Surgical wounds	1033	29	11	-	-	-	-	-	-
Anatol et al. (1997)[¶] [13]	Surgical wounds	-	-	-	49	Not reported	2	138	Not reported	0
Barnett et al. (1998) [14]	Lacerations	62	0	Not reported	-	-	-	49	2	Not reported
Bernard et al. (2001) [15]	Surgical wounds	24	0	0	-	-	-	28	0	0
Brown et al. (2009) [16]	Surgical wounds	64	0	0	-	-	-	70	0	0
Bruns et al. (1998) [11]	Lacerations	42	1	0	-	-	-	-	-	-
Bruns et al. (1996) [17]	Lacerations	30	1	1	-	-	-	31	0	1
Collin et al. (2009) [18]	Surgical wounds	22	0	0	-	-	-	14	0	0
Doraiswamy et al. (2003)[α] [19]	Lacerations	51	Not reported	Not reported	-	-	-	-	-	-
Elmasalme et al. (1995) [31]	Surgical wounds and lacerations	5924	44	0	-	-	-	-	-	-
Ferlise et al. (2001) [20]	Surgical wounds	25	0	0	27	0	0	-	-	-
Halli et al. (2012) [21]	Surgical wounds	30	0	0	-	-	-	30	1	0
Hasan et al. (2009) [34]	Surgical wounds	100	0	3	-	-	-	-	-	-
Knott et al. (2007) [22]	Surgical wounds	11	0	0	-	-	-	11	0	0
Magee et al. (2003) [35]	Surgical wounds	64	0	0	-	-	-	-	-	-
Malhotra et al. (2016) [32]	Surgical wounds	20	0	0	-	-	-	-	-	-
Mattick et al. (2002) [9]	Lacerations	19	0	0	25	0	0	-	-	-
Mourougayan (2006) [36]	Surgical wounds	104	0	0	-	-	-	-	-	-
Ong et al. (2002) [23]	Surgical wounds	26	0	0	-	-	-	33	0	0
Osmond et al. (1999)[β] [24]	Lacerations	82	0	2	-	-	-	-	-	-
Osmond et al. (1995)[δ] [25]	Lacerations	-	-	-	-	-	-	-	-	-
Quinn et al. (1993) [26]	Lacerations	37	1	3	-	-	-	38	1	2
Rajimwale et al. (2004) [7]	Surgical wounds	142	0	0	-	-	-	-	-	-
Resch and Hick (2000) [37]	Lacerations	100	2	1	-	-	-	-	-	-
Romero et al. (2011) [8]	Surgical wounds	23	0	0	24	1	0	-	-	-
Spauwen et al. (2006) [27]	Surgical wounds	15	0	0	-	-	-	15	0	0
van den Ende et al. (2004) [28]	Surgical wounds	50	4	13	-	-	-	50	2	0
Watson (1989) [38]	Lacerations	40	2	0	-	-	-	-	-	-
Wilson and Mercer (2008) [29]	Surgical wounds	186	0	0	121	5	0	-	-	-
Zempsky et al. (2004) [30]	Lacerations	48	1	6	45	0	1	-	-	-
TOTAL		**8400**	**85 (1.0%)**	**40 (0.5%)**	**291**	**6 (2.1%)**	**3 (1.0%)**	**533**	**7 (1.8%)**	**3 (0.6%)**

* Total number of wounds – refers to the number of wounds followed up at the assessment timeframe, not the total number of initially recruited patients/wounds.
¶ Two intervention groups had wounds closed with sutures and the results for both of these groups have been pooled.
α Three intervention groups had wounds closed with TA and the results for all three of these groups have been pooled.
β Two intervention groups had wounds closed with TA and the results for both of these groups have been pooled.
δ This study compared TA with sutures but only reported cost analysis (no clinical data reported).

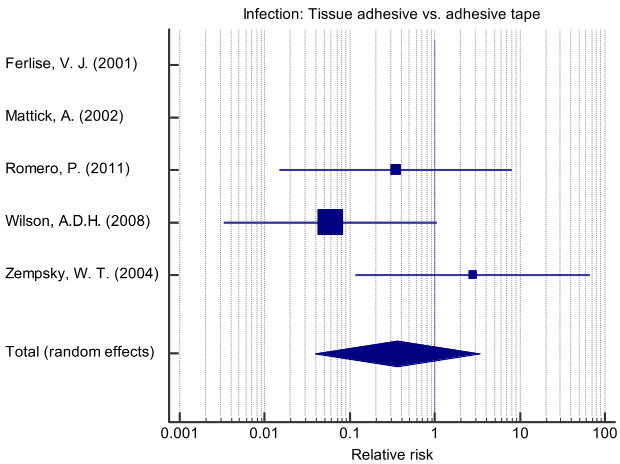

Fig. 4. Forest plot comparing infection risk between TiA and AdT.

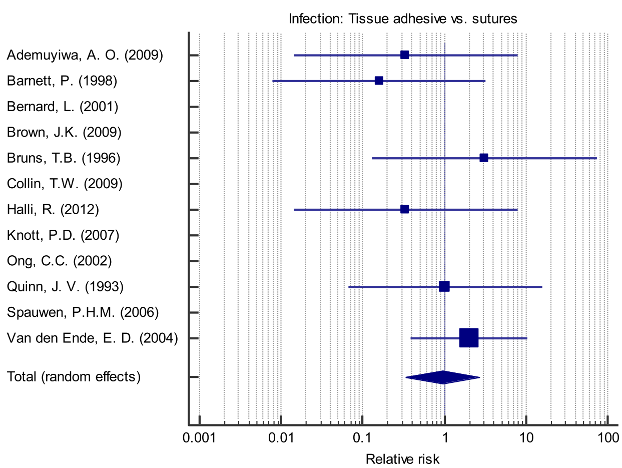

Fig. 5. Forest plot comparing infection risk between TiA and sutures.

2.6. Other complications

Rates of other complications were reported by 27 studies and the overall rates of other complications are summarized in Table 4.

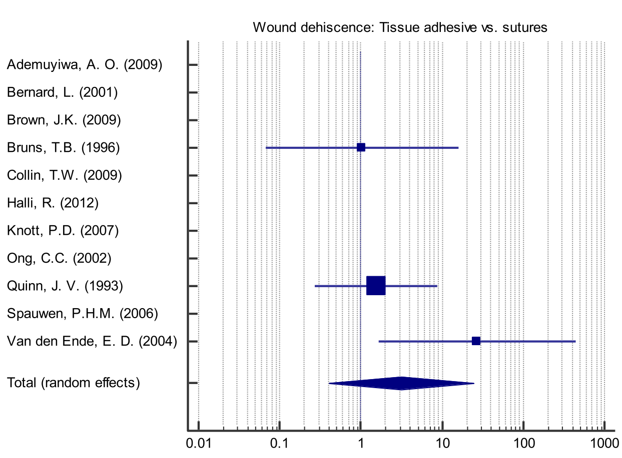

Fig. 6. Forest plot comparing dehiscence risk between TiA and sutures.

2.7. Cost

2.7.1. Non-comparative studies ($n = 2$)

Watson (1989) reported the cost of one application of tissue adhesive to be 45 pence, compared with 90 pence for a 5/0 suture [38]. Rajimwale et al. (2004) reported each vial of Dermabond® tissue adhesive to cost $30.00 [7].

2.7.2. Comparative studies ($n = 10$)

In studies comparing TiA with sutures, TiA was significantly more expensive in 3 studies [15,20,28] but there was no significant difference in total procedure cost [15]. A formal cost-analysis found TiA to be cheaper than dissolving/non-dissolving sutures when accounting for material, medical provider, and health service costs [25] with another paper estimating savings up to £500 per patient undergoing cleft lip repair if TiA was used when factoring for suture removal and associated medical costs [18]. AdT was cheaper than sutures [12]. Another study found TiA to be more expensive than AdT but cheaper than sutures [9] . Comparing different tissue adhesives, octyl-cyanoacrylate (single-use) was 8-fold more expensive per patient than a reusable vial of butyl-cyanoacrylate [24].

3. Discussion

Non-suture techniques are widely used for skin closure in the pediatric population with theoretical benefits including equal tension distribution across the wound, pain-free closure, and no requirement for suture removal [39,40]. However, evidence comparing them directly and with conventional suture closure is conflicting.

Clinician-reported cosmesis of wounds closed with TiA and sutures were similar but AdT had a statistically significant improved cosmetic outcome over TiA. However, it is important to consider that these results were obtained from three randomized trials, and the difference is primarily driven by results of a single study evaluating adjunctive wound closure with sutures TiA/AdT for laparoscopic trocar wounds; the other studies looked at primary closure of lacerations with TiA/AdT alone. Different TiAs did not appear to alter cosmetic outcome. Similar results were obtained in a meta-analysis in adult patients: TiA had equivalent cosmesis to sutured wounds, however, AdT wounds had significantly better cosmetic outcomes over TiA [41]. Wounds closed with AdT also demonstrated similar cosmetic outcomes to sutured wounds [42].

In interpreting our findings for cosmetic outcome, it is important to consider the marked discrepancy which exists between studies in terms of method and time of cosmesis assessment. Whilst the VAS and HWES were used most frequently, other studies utilized alternative scales. Similarly, the timeframe of cosmetic assessment was variable, ranging from 2 to 3 weeks to 2+ years post-procedure. For several studies, only short-term follow-up data were available. Due to this heterogeneity, we opted to pool the data to provide an overall cosmetic outcome.

We identified a low overall wound infection incidence (1.0–2.1%), with no difference amongst techniques. Data comparing AdT with sutures were limited and there were no reported infections in the study comparing butyl-cyanoacrylate with octyl-cyanoacrylate. This suggests that TiA has equivalent risk of infection compared to sutures and AdT. Similar results have been obtained in adults; a 2014 Cochrane review found no difference in infection rates when comparing TiA with sutures or with AdT. However, the analysis was underpowered to detect a significant difference [41]. Gkegkes et al. (2012) also found no difference in infection rates in a meta-analysis comparing AdT with sutures for surgical wound closure in adults [42].

In interpreting our findings, it is important to consider that most studies evaluated clean/uncomplicated wounds which are at low risk of infection. The infection risk in children has been reported between 1.2% and 6.6%, with greater risk in dirty or contaminated wounds [43–46]. Lacerations have a similar post-closure risk of infection in children and adults [47,48]. The low proportion of complicated,

Table 4
Rate of other reported complications in included studies based on skin closure technique.

STUDY	WOUND TYPE/S	TISSUE ADHESIVE		ADHESIVE TAPE		SUTURES	
		Total no. of wounds (n)*	No. of other complications (n)	Total no. of wounds (n)*	No. of other complications (n)	Total no. of wounds (n)*	No. of other complications (n)
Ademuyiwa et al. (2009) [12]	Surgical wounds	26	1	-	-	26	1
Amiel et al. (1999) [33]	Surgical wounds	1033	83	-	-	-	-
Anatol et al. (1997)[¶][13]	Surgical wounds	-	-	49	31[Σ]	138	38[Σ]
Barnett et al. (1998) [14]	Lacerations	Not reported	Not reported	-	-	Not reported	Not reported
Bernard et al. (2001) [35]	Surgical wounds	24	5	-	-	28	3
Brown et al. (2009) [16]	Surgical wounds	64	5	-	-	70	5
Bruns et al. (1998) [11]	Lacerations	42	1	-	-	-	-
Bruns et al. (1996) [17]	Lacerations	30	1	-	-	31	0
Collin et al. (2009) [18]	Surgical wounds	22	1	-	-	14	1
Doraiswamy et al. (2003)[α] [19]	Lacerations	51	10	-	-	-	-
Elmasalme et al. (1995) [31]	Surgical wounds and lacerations	5924	4	-	-	-	-
Ferlise et al. (2001) [20]	Surgical wounds	25	3	27	0	-	-
Halli et al. (2012) [21]	Surgical wounds	30	0	-	-	30	0
Hasan et al. (2009) [34]	Surgical wounds	100	0	-	-	-	-
Knott et al. (2007) [22]	Surgical wounds	11	0	-	-	11	2
Magee et al. (2003) [35]	Surgical wounds	64	5	-	-	-	-
Malhotra et al. (2016) [32]	Surgical wounds	20	2	-	-	-	-
Mattick et al. (2002) [9]	Lacerations	0	0	0	0	-	-
Mourougayan (2006) [36]	Surgical wounds	104	5	-	-	-	-
Ong et al. (2002) [23]	Surgical wounds	26	0	-	-	33	0
Osmond et al. (1999) [24]	Lacerations	Not reported	Not reported	-	-	-	-
Osmond et al. (1995)[δ] [25]	Lacerations	-	-	-	-	-	-
Quinn et al. (1993) [26]	Lacerations	37	1	-	-	38	4
Rajimwale et al. (2004) [7]	Surgical wounds	142	1	-	-	-	-
Resch and Hick (2000) [37]	Lacerations	100	6	-	-	-	-
Romero et al. (2011) [8]	Surgical wounds	23	2	24	1	-	-
Spauwen et al. (2006)[λ] [27]	Surgical wounds	15	8	-	-	15	13
van den Ende et al. (2004) [28]	Surgical wounds	50	12	-	-	50	3
Watson (1989) [38]	Lacerations	40	3	-	-	-	-
Wilson and Mercer (2008) [29]	Surgical wounds	186	33	121	22	-	-
Zempsky et al. (2004) [30]	Lacerations	Not reported	Not reported	Not reported	Not reported	-	-
TOTAL		**8189**	**184 (2.2%)**	**221**	**54 (24.4%)**	**484**	**70 (14.5%)**

* Total number of wounds – refers to the number of wounds followed up at the assessment timeframe, not the total number of initially recruited patients/wounds.
¶ Two intervention groups had wounds closed with sutures and the results for both of these groups have been pooled.
Σ Some wounds had >1 complication (34 sutured wounds and 21 taped wounds had a complication) but as it is unclear which wounds were affected, a total number of complications has been reported.
α Three intervention groups had wounds closed with TA and the results for all three of these groups have been pooled.
δ This study compared TA with sutures but only reported cost analysis (no clinical data reported).
λ Some wounds had overlapping complications at the two wound assessment timepoints but it was not clarified for which wounds this occurred, hence all reported complications were counted.

contaminated wounds may have contributed to the low overall infection rate, masking a potential difference existing between skin closure techniques. Indeed, in animal models, wounds closed with TiA have been significantly less likely to become infected than sutured wounds [49]. TiAs have been established to have antimicrobial properties, particularly inhibiting Gram-positive bacterial growth [50], and once polymerized, seal the wound forming a barrier against external contamination [51,52]. The use of microporous AdT such as Steri-Strips™ appears to have mixed results in terms of microbial contamination. Following application of microporous tape to the skin, at 24 h, there was no difference in the number of bacteria on the skin compared to uncovered skin but at 48 h, there were significantly more bacteria on skin covered by tape [53]. However, Kolt (2003) reported that surgical tapes inhibit bacterial growth which clinically translates into a lower wound infection rate [39].

Wound dehiscence occurred at a similar incidence in the three groups (0.5–1.0%). There was insufficient data to compare the overall incidence of dehiscence in comparative studies evaluating TiA and AdT. There was no difference in wound dehiscence between sutured and glued wounds. It was unclear if there was a significant difference in dehiscence risk when comparing AdT with sutures due to limited data, and there was no difference in dehiscence rate when comparing octyl-cyanoacrylate with butyl-cyanoacrylate. In contrast, a meta-analysis of adult patients found surgical wounds closed with TiA were 3.35-fold more likely to dehisce than sutured wounds. No significant difference was established in dehiscence risk between wounds closed with TiA and AdT, however, the analysis was underpowered [41]. Gkegkes and colleagues (2012) found no difference in risk of dehiscence when comparing taped wounds with sutured wounds in adult surgical patients [42].

Wound dehiscence is an infrequent complication in children, occurring in less than 1% of surgical patients following intra-abdominal surgery [54,55]. Given the majority of included studies in our systematic review evaluated small low-tension wounds, the low incidence of dehiscence is not unexpected. One included study specifically compared octyl-cyanoacrylate with sutures for closure of high-tension excisional wounds but did not identify a difference in the frequency of dehiscence [14]. Another consideration in interpreting these results is the use of TiA and/or AdT for skin closure as an adjunct to sutures occurring in 9 studies. This may convey additional tensile strength and potentially decrease dehiscence risk. The use of TiA has typically been confined to low-tension, small lacerations [56] which could be secondary to concerns over poor tensile strength and hence inflexible wound closure with the initial cyanoacrylates. Newer adhesives such as octyl-cyanoacrylate convey greater tensile strength and are more flexible [2,56]. This has increased the scope of their use: octyl-cyanoacrylate has been successfully used for the management of long (≥4 cm) surgical wounds in adults [57] and in high-tension wounds in children with adjuvant AdT and splints for immobilization [58]. The use of AdT has similarly been limited to closure of low tension wounds [2] due to the weak tensile strength they convey and the risk of loss of adhesion to the skin, predisposing to dehiscence [4,59]. However, adjunctive chemical adhesives such as Mastisol can be used to reinforce the tape and ensure greater longevity of adherence [3]. Animal studies comparing the wound bursting strength of wounds closed with TiA and AdT have demonstrated that significantly greater amounts of pressure are required to compromise wounds closed with TiA compared to taped wounds [60].

This systematic review and meta-analysis has some limitations. Firstly, no pediatric study to date has directly compared TiA with AdT and sutures. This has limited our ability to compare these three alternatives and conclusions which have been drawn rely on indirectly comparing these techniques with one another. Secondly, the majority of included studies have small sample sizes and are at high-risk of bias. The bulk of the available evidence is confined to case series and a small number of comparative studies, several of which are retrospective in nature. These studies were often statistically underpowered to detect differences between intervention arms in endpoints such as wound infection and wound dehiscence. Thirdly, a few included studies utilized TiA and/or AdT in addition to sutures for skin closure. Given the small number of studies which assessed this, for the purposes of this study, they were not evaluated as a separate wound closure technique. This alternative use of combination skin closure requires further assessment to ascertain whether it conveys any additional advantages to skin closure with TiA or AdT alone.

4. Conclusions

TiA, AdT, and sutures are safe alternatives for skin closure of wounds in children. Current evidence suggests that these techniques have a similar risk of wound infection and dehiscence. AdT appears to convey better cosmetic outcome; however, this finding is drawn from three randomized trials with heterogenous techniques, assessing different wound types, and with only a single trial driving the results in favor of AdT. Given most comparative studies are small size with high-risk of bias and adult studies have shown significantly higher risk of dehiscence in wounds closed with TiA compared to sutures, further adequately powered randomized controlled trials are required to verify these findings. There is requirement for these randomized studies to directly compare these three techniques and also assess the role of adjunct skin closure with sutures and TiA/AdT to ascertain whether this conveys any benefits over skin closure with TiA or AdT alone.

Appendix A. Search Strategy

((("tissue adhesive" OR "adhesive glue" OR "Dermabond" OR "Liquiband" OR "Histoacryl" OR "Glubran" OR "Indermil" OR "cyanoacrylate" OR "glue" OR "octylcyanoacrylate*" OR "enbucrilate" OR "butylcyanoacrylate*" OR "acrylate*" OR "bucrylate*"OR "Fibrin Tissue Adhesive" OR "adhesive tape" OR "surgical tape" OR "adhesive strip" OR "SteriStrip*"OR "Steri-Strip*" OR "tape" OR "sutureless" OR "sutureless")) AND ("Pediatric*" OR "pediatric*" OR "child*")) AND ("Wounds and Injuries" OR "wound closure" OR "Wound Closure Techniques" OR "skin closure" OR "laceration" OR "surgical wound" OR "incision")

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